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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/669,158	09/22/2003	Edward A. Neuwelt	720109.401	1678

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EXAMINER	
ARNOLD, ERNST V	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 08/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/669,158	NEUWELT ET AL.	
	Examiner	Art Unit	
	Ernst V. Arnold	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-25 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-25 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on 16 March 2004 is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 4/19/04.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Application 10/669,158 filed on 9/22/2003 claims benefit of 60/412,494 filed on 9/20/2002 and benefit of 60/478,383 filed on 6/13/2003.

The new Examiner of record acknowledges receipt of Applicant's response to the restriction requirement filed on 5/3/2006. Applicant elected the species N-acetylcysteine for examination. The claims will be examined to the extent that they read upon N-acetylcysteine. Claims 1-25 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a reducing an ischemia-reperfusion injury, does not reasonably provide enablement for preventing an ischemia-reperfusion injury. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims without an undue amount of experimentation.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: 1) scope or breadth

of the claims; 2) nature of the invention; 3) relative level of skill possessed by one of ordinary skill in the art; 4) state of, or the amount of knowledge in, the prior art; 5) level or degree of predictability, or a lack thereof, in the art; 6) amount of guidance or direction provided by the inventor; 7) presence or absence of working examples; and 8) quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure. When the above factors are weighed, it is the Examiner's position that one skilled in the art could not practice the invention without undue experimentation.

1) Scope or breadth of the claims

The claims are broader in scope than the enabling disclosure. The specification merely discloses, without more, that a method of reducing ischemia-reperfusion injury. However, Applicant is purporting a method to prevent ischemia-reperfusion injury.

2) Nature of the invention

The nature of the invention is directed to a method of reducing ischemia-reperfusion injury.

3) Relative level of skill possessed by one of ordinary skill in the art

The relative level of skill possessed by one of ordinary skill in the art of medical research is relatively high, as a majority of lead investigators directing scientific research and development in this particular technological area possess an M.D. and/or a Ph.D. in a scientific discipline such as organic synthetic chemistry, medicinal chemistry, biochemistry, pharmacology, biology or the like and technicians performing the work with Masters, Bachelors and high school diplomas.

4) State of, or the amount of knowledge in, the prior art

The art teaches that a stroke (ischemia-reperfusion injury) is a medical emergency and to help prevent a stroke lifestyle changes are recommended (Medline Plus Medical Encyclopedia: stroke 6/27/05 pages 3 and 5).

5) Level or degree of predictability, or a lack thereof, in the art

A high degree of unpredictability existed in the state of the prior art regarding how to prevent ischemia-reperfusion injury (stroke). These are primarily lifestyle changes such as blood pressure screening, cholesterol checks, quit smoking, exercise, and weight loss (Medline Plus Medical Encyclopedia: stroke 6/27/05 page 5) but the art does not recognize absolute preventative measures.

6) Amount of guidance or direction provided by the inventor

Applicant was required to provide in the specification additional guidance and direction with respect to how use the claimed subject matter in order for the application to be enabled with respect to the full scope of the claimed invention. Although the instant specification discloses a method of reducing an ischemia-reperfusion injury, it does not disclose a method for preventing ischemia-reperfusion injury.

7) Presence or absence of working examples

The specification fails to provide scientific data and working embodiments with respect to a method of preventing ischemia-reperfusion injury.

8) Quantity of experimentation required to make and use the claimed invention based upon the content of the supporting disclosure

As a result, one of ordinary skill in the art would be required to conduct an undue amount of experimentation to reasonably and accurately determine whether the composition and corresponding method of the instant application does in fact prevent ischemia-reperfusion.

Genetech, 108 F.3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Accordingly the claims are evaluated as a method for reducing an ischemia-reperfusion injury and not a method for preventing an ischemia-reperfusion injury.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7, 14, 15, 17, 18, 24 and 25 are rejected under 35 U.S.C. 102(b) as being anticipated by Singh (5,912,019).

Singh discloses methods of minimizing ischemic insult to an organ or skeletal tissue of a subject comprising contacting the organ or tissue with an inhibitor of iNOS (N-acetyl-cysteine) (Claims 1 and 2). Singh disloses that animals were treated with N-acetyl-cysteine before and after the onset of ischemia (Column 7, liens 35-41). Singh

discloses that the method can be performed intraarterial, intravenous, subcutaneous or intramuscular injections thus anticipating instant claims 1, 3-5, 14, and 17 and (column 5, lines 60-65). Singh discloses that a preferred dosage is from about 100 to about 300 mg/kg body weight (Column 5, lines 39-42). Please note that USPTO is not equipped with the scientific instruments needed to measure they myriad number of ways of expressing concentrations such as determining if the disclosure of Singh results in a serum concentration of the scavenger from about 1mM to 40 mM. It is the Examiner's position that the dosage disclosed by Singh reads upon the instantly claimed concentration range and the burden is shifted to Applicant to demonstrate otherwise. Singh discloses that the method may also be used where ischemic conditions are induced by infarctions and it is the Examiner's position that the infarct size would be reduced (Column 4, lines 55-57). Singh defines organ as including the brain and thus reads on claim 7. It is the Examiner's position that the blood will carry the scavenger to the central nervous system and thus anticipate instant claim 18.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Singh (5,912,019) in view of Andersen (Perfusion 1995, 10, 21-26).

Applicant claims a method for preventing or reducing an ischemia-repefusion injury, comprising administering to a subject in need thereof an effective amount of a free radical scavenger intra-arterially or intravenously prior to, concurrently with, or following reperfusion.

Determination of the scope and content of the prior art

(MPEP 2141.01)

The reference of Singh is desribed in detail above and that discussion is hereby incorporated by reference.

Andersen teaches the role of N-acetylcysteine administration during cardiopulmonary bypass (Abstract). Andersen teaches that patients received a bolus of 100 mg/kg N-acetylcysteine followed by a continuous infusion of 20 mg/kg via the reservoir of the bypass circuit from the beginning to the end of the cardiopulmonary bypass (Page 22, Patients and methods). Andersen teaches that N-acetylcysteine may

be used safely alone or in conjunction with other therapies, which aim to minimize reperfusion injuries (Page 26, second paragraph).

Ascertainment of the difference between the prior art and the claims (MPEP 2141.02)

Singh does not expressly teach a method for preventing or reducing an ischemia-repefusion injury, comprising administering to a subject in need thereof an effective amount of a free radical scavenger intra-arterially or intravenously prior to, concurrently with, or following reperfusion;

1. wherein the ischemia-reperfusion injury is a cerebral injury, cognitive dysfunction or cerebral hemorrhage.

2. wherein the ischemia-reperfusion injury is associated with cardiopulmonary bypass procedure.

Finding of prima facie obviousness

Rational and Motivation (MPEP 2142-2143)

1. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use the method of Singh for reducing an ischemia-repefusion injury, comprising administering to a subject in need thereof an effective amount of a free radical scavenger, N-acetyl-cysteine, intra-arterially or intravenously prior to, concurrently with, or following reperfusion; wherein the ischemia-reperfusion injury is a cerebral injury, cognitive dysfunction or cerebral hemorrhage.

One of ordinary skill in the art would have been motivated to do this because Singh teaches that the method may be employed upon occurrences of various traumas

to the central nervous sytem, cerebral hemorrhage, stroke, and temporary occlusion of blood vessels.

2. It would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to use the method of Singh for reducing an ischemia-repefusion injury wherein the ischemia-reperfusion injury is associated with a cardiopulmonary bypass procedure as suggested by Andersen and produce the instant invention.

One of ordinary skill in the art would have been motivated to do this because Andersen teaches the cardiopulmonary bypass results in reperfusion injuries (Page 21, introduction) and the method of Singh would reduce these injuries. The adjustment of particular working conditions (e.g., the method of administration, the time of administration and the amount of the N-acetyl-cysteine administered) is deemed merely a matter of routine optimization which is within the skill of one of ordinary skill in the art.

In the absence of any criticality/unexpected results, the presently claimed invention is considered prima facie obvious over the prior art for the reasons of record and those stated above.

A reference is good not only for what it teaches by direct anticipation but also for what one of ordinary skill in the art might reasonably infer from the teachings. (*In re Opprecht* 12 USPQ 2d 1235, 1236 (Fed Cir. 1989); *In re Bode* 193 USPQ 12 (CCPA) 1976).

A prior art disclosure is not limited to its working examples or to its preferred embodiments. (Merck & Co. Inc. v. Biocraft Labs. Inc., 874 F.2d 804, 807, 10 USPQ2d

1843, 1846 (Fed. Cir. 1989); *In re Fracalossi* 681 F.2d 792, 794 n. 1, 215 USPQ 569, 570 n.1 (CCPA 1982); *In re Lamberti*, 545 F.2d 747, 750, 192 USPQ 278, 280 (CCPA 1976); *In re Boe*, 355 F.2d 961, 965, 148 USPQ 507, 510 (CCPA 1996).

Accordingly, the burden of proof is upon Applicants to show that the instantly claimed subject matter is different and unobvious over those taught by the prior art. (See: *In re Brown*, 173 USPQ 685, 688; *In re Best*, 195 USPQ 430 and *In re Marosi*, 218 USPQ 289, 293).

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Conclusion

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ernst V. Arnold whose telephone number is 571-272-8509. The examiner can normally be reached on M-F (6:15 am-3:45 pm).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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